Available online at www.sciencedirect.com
ScienceDirect
Psychiatry Research 149 (2007) 273–277
PSYCHIATRY RESEARCH
www.elsevier.com/locate/psychres

Brief report

Negative association between a history of obstetric complications and the number of neurological soft signs in first-episode schizophrenic disorder

Marco P.M. Boks [a,*], Jean-Paul Selten [a], Stuart Leask [b], Stynke Castelein [c], Robert J. van den Bosch [c]

[a] *Rudolf Magnus Institute of Neuroscience, Department of Psychiatry B01.206, University Medical Centre Utrecht, PO Box 85500, 3508 GA Utrecht, The Netherlands*
[b] *University of Nottingham, Division of Psychiatry, Duncan Macmillan House, Porchester Road, Nottingham NG3 6AA, United Kingdom*
[c] *Department of Psychiatry, University Medical Centre Groningen, University of Groningen, PO Box 30.001, 9700 RB Groningen, The Netherlands*

Received 31 March 2005; received in revised form 25 November 2005; accepted 17 April 2006

Abstract

We examined the relationship between a history of obstetric complications (OCs) and the number of neurological soft signs (NSS) in a group of 132 patients experiencing their first episode of psychosis. We measured NSS by means of a comprehensive standardized assessment and gained information on a selection of nine OCs from the patient's mother. Contrary to our expectations we found significantly more NSS in the group of patients without a history of OCs. This effect was independent of medication in the group of patients with a schizophrenic disorder, but not in the entire group. It is possible that the patients with a history of OCs carry fewer genes for schizophrenia (and NSS) and 'needed' the OCs to develop schizophrenia.

Keywords: Psychosis; Schizophrenia; Neurodevelopmental; Neurological abnormalities; Development

1. Introduction

There is compelling evidence of an increased number of neurological soft signs (NSS) in first-episode psychosis (Dazzan and Murray, 2002) and schizophrenia (Boks et al., 2000; Leask et al., 2002). These minor neurological abnormalities are thought to reflect a disturbance in neurodevelopment. Furthermore, several studies suggest that NSS are associated with an increased ventricle-to-brain ratio in first-episode psychosis and schizophrenia (Wright et al., 2000; DeMyer et al., 1988; Rubin et al., 1994). However, the exact aetiology of NSS in schizophrenia remains obscure. One possible explanation for the increase of NSS in first-episode psychosis and schizophrenia is the surplus of obstetric complications (OCs), since OCs have been reported to be associated with minor neurological abnormalities in the pediatric literature (Hertzig, 1981). Furthermore, a relationship has been found between OCs and brain abnormalities such as ventricular enlargement (Lewis and Murray, 1987; McNeil et al., 2000).

* Corresponding author. Tel.: +31 30 2506370; fax: +31 30 2505509.
E-mail addresses: m.p.m.boks@psych.azu.nl (M.P.M. Boks), j.p.selten@azu.nl (J.-P. Selten), stuart.leask@nottingham.ac.uk (S. Leask), s.castelein@psy.umcg.nl (S. Castelein), r.j.van.den.bosch@med.rug.nl (R.J. van den Bosch).

0165-1781/$ - see front matter © 2006 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.psychres.2006.04.008

The observation that both NSS and OCs are associated with an increased ventricle-to-brain ratio (Wright et al., 2000) and that OCs are associated with NSS in children lead to the hypothesis that OCs contribute to the development of NSS. Therefore we tested the hypothesis that a history of OCs is related to a greater number of NSS in patients with a first psychotic episode.

2. Methods

Between 1998 and 2000, we examined 132 consecutive inpatients and outpatients with a first-episode psychosis to the University Medical Centre Groningen, the Netherlands. The sample included 92 patients with a diagnosis of a 'schizophrenic disorder' (DSM-IV: 295.x: schizophrenia, schizophreniform or schizo-affective disorder). The patients had been diagnosed with schizophrenia ($N=47$), schizo-affective disorder ($N=20$), schizophreniform disorder ($N=25$), drug-induced psychotic disorder ($N=10$), brief psychotic disorder ($N=10$), psychotic disorder not otherwise specified ($N=7$), mood disorder with psychotic features ($N=9$), delusional disorder ($N=4$). Eighty-three patients (63%) were male, and the mean age was 25.9 years (S.D. 5.8). Thirty-two patients were not on antipsychotics. The other patients used olanzapine ($N=32$), risperidone ($N=31$), pimozide ($N=10$), quetiapine ($N=8$), haloperidol ($N=5$), zuclopenthixol ($N=5$), sertindole ($N=3$), clozapine ($N=2$), perphenazine ($N=2$), and penfluridol ($N=1$). The mean dosage in haloperidol equivalents was 4.1 mg (S.D. 3.4). Ten patients (8%) were left-handed, and in five patients (4%) handedness was mixed. Seventeen patients (13%) had a history of head trauma or another neurological disorder. Patients with learning disabilities or a primary diagnosis of addiction as assessed by the responsible medical officer were excluded.

After complete description of the study, written informed consent was obtained. DSM-IV diagnoses were established by means of the SCAN (Schedules for Clinical Assessment in Neuropsychiatry) interview (Wing et al., 1990). Information on handedness and history of head trauma was assessed in a semi-structured interview. Six weeks after inclusion, all patients underwent a standardized comprehensive neurological investigation, the Cambridge Neurological Investigation (CNI) (Chen et al., 1995). This inventory is the most comprehensive of NSS assessments and includes 76 NSS, most NSS from the Neurological Evaluation Scale (Buchanan and Heinrichs, 1989) along with other NSS. Three trainees in psychiatry and one neurologist conducted the examinations. Interrater reliability was assessed in 40 subjects and was good (intraclass correlation for the total score=0.83). Raters were blind to the OC score but not to the diagnosis. Previously we reported a significant increase in the number of NSS in patients versus healthy controls (Boks et al., 2004).

The biological mother completed a standardized questionnaire on several pregnancy, labor-delivery and neonatal complications. All but eight mothers were of Dutch origin and had delivered in the Netherlands. The remaining mothers were Turkish ($N=1$), Sudanese ($N=1$), Russian ($N=2$) or Surinamese ($N=4$) and had given birth in their country of origin. The mean age of the mothers at delivery was 28.3 years (S.D. 8.1), and the mean number of previous deliveries was 1.5 (S.D. 1.6). We focused on the nine OCs from our questionnaire that had been shown to be significant risk factors for schizophrenia in the Cannon et al. (2002) meta-analysis: diabetes in pregnancy, birth weight <2000 g and birth weight <2500 g separately, emergency Cesarean section, uterine atony, rhesus antagonism, asphyxia, bleeding in pregnancy, and pre-eclampsia.

We tested differences in the number of NSS between groups with and without OCs using an independent two-tailed *t*-test. The analyses were conducted for the entire group of first-episode patients and for the subgroups of schizophrenic disorders and other psychotic disorders separately.

We also tested whether the presence of a particular OC was associated with the total number of NSS using a chi-square test or, when appropriate, a Fisher exact test. For those OCs that were related to the total number of NSS, we tested the association between the OC and the categories of NSS from the CNI by means of a Mann–Whitney *U*-test. Because this analysis served as an exploration of potential relationships only, we did not correct for multiple comparison. Finally, we investigated whether the differences in the dosage of antipsychotics accounted for the differences between patients with and without a history of OCs by using a general linear model with the dosage in haloperidol equivalents as a covariate.

3. Results

Table 1 presents the clinical and demographic data on patients with and without a history of OCs. There were no significant differences between the two groups in age, sex, dosage of antipsychotics, history of neurological illness or head trauma, handedness or maternal age at delivery. The prevalence rates of the OCs were as follows: diabetes in pregnancy ($N=10$, 7.5%), birth weight <2000 g ($N=6$, 4.5%) and birth weight <2500 g ($N=3$, 2.3%), emergency Cesarean section ($N=2$,